

NR<sup>10</sup>- (wherein R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl), and R<sup>5</sup> is selected from one of the following twenty-two groups:

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- 1) hydrogen, oxiranylC<sub>1-4</sub>alkyl or C<sub>1-5</sub>alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, chloro, bromo and amino;
  - 2) C<sub>1-5</sub>alkylX<sup>2</sup>C(O)R<sup>11</sup> (wherein X<sup>2</sup> represents -O- or -NR<sup>12</sup>- (in which R<sup>12</sup> represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>11</sup> represents C<sub>1-3</sub>alkyl, -NR<sup>13</sup>R<sup>14</sup> or -OR<sup>15</sup> (wherein R<sup>13</sup>, R<sup>14</sup> and R<sup>15</sup> which may be the same or different each represents hydrogen, C<sub>1-5</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl));
  - 3) C<sub>1-5</sub>alkylX<sup>3</sup>R<sup>16</sup> (wherein X<sup>3</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -OC(O)-, -NR<sup>17</sup>C(O)-, -C(O)NR<sup>18</sup>-, -SO<sub>2</sub>NR<sup>19</sup>-, -NR<sup>20</sup>SO<sub>2</sub>- or -NR<sup>21</sup>- (wherein R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>16</sup> represents hydrogen, C<sub>1-3</sub>alkyl, cyclopentyl, cyclohexyl or a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C<sub>1-3</sub>alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C<sub>1-4</sub>alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cyanoalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>aminoalkyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkoxy, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkoxy and a group -(O-)<sub>f</sub>(C<sub>1-4</sub>alkyl)<sub>g</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl));
  - 4) C<sub>1-5</sub>alkylX<sup>4</sup>C<sub>1-5</sub>alkylX<sup>5</sup>R<sup>22</sup> (wherein X<sup>4</sup> and X<sup>5</sup> which may be the same or different are each -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>23</sup>C(O)-, -C(O)NR<sup>24</sup>-, -SO<sub>2</sub>NR<sup>25</sup>-, -NR<sup>26</sup>SO<sub>2</sub>- or -NR<sup>27</sup>- (wherein R<sup>23</sup>, R<sup>24</sup>, R<sup>25</sup>, R<sup>26</sup> and R<sup>27</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>22</sup> represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl);
  - 5) R<sup>28</sup> (wherein R<sup>28</sup> is a 4-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cyanoalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>aminoalkyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkoxy, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkoxy and a group -(O-)<sub>f</sub>(C<sub>1-4</sub>alkyl)<sub>g</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl));

$\text{C}_{1-4}\text{alkylsulphonylC}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkoxycarbonyl}$ ,  $\text{C}_{1-4}\text{aminoalkyl}$ ,  $\text{C}_{1-4}\text{alkylamino}$ ,  $\text{di}(\text{C}_{1-4}\text{alkyl})\text{amino}$ ,  $\text{C}_{1-4}\text{alkylaminoC}_{1-4}\text{alkyl}$ ,  $\text{di}(\text{C}_{1-4}\text{alkyl})\text{aminoC}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkylaminoC}_{1-4}\text{alkoxy}$ ,  $\text{di}(\text{C}_{1-4}\text{alkyl})\text{aminoC}_{1-4}\text{alkoxy}$  and a group  $\text{-}(\text{-O-})_f(\text{C}_{1-4}\text{alkyl})_g\text{ringD}$  (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from  $\text{C}_{1-4}\text{alkyl}$ ));

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- 6)  $\text{C}_{1-5}\text{alkylR}^{28}$  (wherein R<sup>28</sup> is as defined hereinbefore);
  - 7)  $\text{C}_{2-5}\text{alkenylR}^{28}$  (wherein R<sup>28</sup> is as defined hereinbefore);
  - 8)  $\text{C}_{2-5}\text{alkynylR}^{28}$  (wherein R<sup>28</sup> is as defined hereinbefore);
  - 9) R<sup>29</sup> (wherein R<sup>29</sup> represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents selected from hydroxy, halogeno, amino,  $\text{C}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkoxy}$ ,  $\text{C}_{1-4}\text{hydroxyalkyl}$ ,  $\text{C}_{1-4}\text{aminoalkyl}$ ,  $\text{C}_{1-4}\text{alkylamino}$ ,  $\text{C}_{1-4}\text{hydroxyalkoxy}$ , carboxy, trifluoromethyl, cyano, -C(O)NR<sup>30</sup>R<sup>31</sup>, -NR<sup>32</sup>C(O)R<sup>33</sup> (wherein R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup> and R<sup>33</sup>, which may be the same or different, each represents hydrogen,  $\text{C}_{1-4}\text{alkyl}$  or  $\text{C}_{1-3}\text{alkoxyC}_{2-3}\text{alkyl}$ ) and a group  $\text{-}(\text{-O-})_f(\text{C}_{1-4}\text{alkyl})_g\text{ringD}$  (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from  $\text{C}_{1-4}\text{alkyl}$ ));
  - 10)  $\text{C}_{1-5}\text{alkylR}^{29}$  (wherein R<sup>29</sup> is as defined hereinbefore);
  - 11)  $\text{C}_{2-5}\text{alkenylR}^{29}$  (wherein R<sup>29</sup> is as defined hereinbefore);
  - 12)  $\text{C}_{2-5}\text{alkynylR}^{29}$  (wherein R<sup>29</sup> is as defined hereinbefore);
  - 13)  $\text{C}_{1-5}\text{alkylX}^6\text{R}^{29}$  (wherein X<sup>6</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>34</sup>C(O)-, -C(O)NR<sup>35</sup>-, -SO<sub>2</sub>NR<sup>36</sup>-, -NR<sup>37</sup>SO<sub>2</sub>- or -NR<sup>38</sup>- (wherein R<sup>34</sup>, R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup> and R<sup>38</sup> each independently represents hydrogen,  $\text{C}_{1-3}\text{alkyl}$  or  $\text{C}_{1-3}\text{alkoxyC}_{2-3}\text{alkyl}$ ) and R<sup>29</sup> is as defined hereinbefore);
  - 14)  $\text{C}_{2-5}\text{alkenylX}^7\text{R}^{29}$  (wherein X<sup>7</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>39</sup>C(O)-, -C(O)NR<sup>40</sup>-, -SO<sub>2</sub>NR<sup>41</sup>-, -NR<sup>42</sup>SO<sub>2</sub>- or -NR<sup>43</sup>- (wherein R<sup>39</sup>, R<sup>40</sup>, R<sup>41</sup>, R<sup>42</sup> and R<sup>43</sup> each independently represents hydrogen,  $\text{C}_{1-3}\text{alkyl}$  or  $\text{C}_{1-3}\text{alkoxyC}_{2-3}\text{alkyl}$ ) and R<sup>29</sup> is as defined hereinbefore);

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- 15)  $C_{2-5}\text{alkynyl}X^8R^{29}$  (wherein  $X^8$  represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>44</sup>C(O)-, -C(O)NR<sup>45</sup>-, -SO<sub>2</sub>NR<sup>46</sup>-, -NR<sup>47</sup>SO<sub>2</sub>- or -NR<sup>48</sup>- (wherein R<sup>44</sup>, R<sup>45</sup>, R<sup>46</sup>, R<sup>47</sup> and R<sup>48</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>29</sup> is as defined hereinbefore);
  - 16)  $C_{1-4}\text{alkyl}X^9C_{1-4}\text{alkyl}R^{29}$  (wherein X<sup>9</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>49</sup>C(O)-, -C(O)NR<sup>50</sup>-, -SO<sub>2</sub>NR<sup>51</sup>-, -NR<sup>52</sup>SO<sub>2</sub>- or -NR<sup>53</sup>- (wherein R<sup>49</sup>, R<sup>50</sup>, R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>29</sup> is as defined hereinbefore);
  - 17)  $C_{1-4}\text{alkyl}X^9C_{1-4}\text{alkyl}R^{28}$  (wherein X<sup>9</sup> and R<sup>28</sup> are as defined hereinbefore);
  - 18) C<sub>2-5</sub>alkenyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, amino, C<sub>1-4</sub>alkylamino, N,N-di(C<sub>1-4</sub>alkyl)amino, aminosulphonyl, N-C<sub>1-4</sub>alkylaminosulphonyl and N,N-di(C<sub>1-4</sub>alkyl)aminosulphonyl;
  - 19) C<sub>2-5</sub>alkynyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, amino, C<sub>1-4</sub>alkylamino, N,N-di(C<sub>1-4</sub>alkyl)amino, aminosulphonyl, N-C<sub>1-4</sub>alkylaminosulphonyl and N,N-di(C<sub>1-4</sub>alkyl)aminosulphonyl;
  - 20)  $C_{2-5}\text{alkenyl}X^9C_{1-4}\text{alkyl}R^{28}$  (wherein X<sup>9</sup> and R<sup>28</sup> are as defined hereinbefore);
  - 21)  $C_{2-5}\text{alkynyl}X^9C_{1-4}\text{alkyl}R^{28}$  (wherein X<sup>9</sup> and R<sup>28</sup> are as defined hereinbefore); and
  - 22)  $C_{1-4}\text{alkyl}R^{54}(C_{1-4}\text{alkyl})_q(X^9)_rR^{55}$  (wherein X<sup>9</sup> is as defined hereinbefore, q is 0 or 1, r is 0 or 1, and R<sup>54</sup> and R<sup>55</sup> are each independently selected from hydrogen, C<sub>1-3</sub>alkyl, cyclopentyl, cyclohexyl and a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C<sub>1-3</sub>alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C<sub>1-4</sub>alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cyanoalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>aminoalkyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkoxy, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkoxy and a group -(O-)(C<sub>1-4</sub>alkyl)<sub>f</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl), with the proviso that R<sup>54</sup> cannot be hydrogen);

and additionally wherein any C<sub>1-5</sub>alkyl, C<sub>2-5</sub>alkenyl or C<sub>2-5</sub>alkynyl group in R<sup>5</sup>X<sup>1-</sup> may bear one or more substituents selected from hydroxy, halogeno and amino);

$R^1$  represents hydrogen, oxo, halogeno, hydroxy,  $C_{1-4}$ alkoxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxymethyl,  $C_{1-4}$ alkanoyl,  $C_{1-4}$ haloalkyl, cyano, amino,  $C_{2-5}$ alkenyl,  $C_{2-5}$ alkynyl,  $C_{1-3}$ alkanoyloxy, nitro,  $C_{1-4}$ alkanoylamino,  $C_{1-4}$ alkoxycarbonyl,  $C_{1-4}$ alkylsulphanyl,  $C_{1-4}$ alkylsulphinyl,  $C_{1-4}$ alkylsulphonyl, carbamoyl,  $N$ - $C_{1-4}$ alkylcarbamoyl,  $N,N$ -di( $C_{1-4}$ alkyl)carbamoyl, aminosulphonyl,  $N$ - $C_{1-4}$ alkylaminosulphonyl,  $N,N$ -di( $C_{1-4}$ alkyl)aminosulphonyl,  $N$ -( $C_{1-4}$ alkylsulphonyl)amino,  $N$ -( $C_{1-4}$ alkylsulphonyl)- $N$ -( $C_{1-4}$ alkyl)amino,  $N,N$ -di( $C_{1-4}$ alkylsulphonyl)amino, a  $C_{3-7}$ alkylene chain joined to two ring C carbon atoms,  $C_{1-4}$ alkanoylamino $C_{1-4}$ alkyl, carboxy or a group  $R^{56}X^{10}$  (wherein  $X^{10}$  represents a direct bond, -O-, - $CH_2$ -, -OC(O)-, -C(O)-, -S-, -SO-, - $SO_2$ -, -NR<sup>57</sup>C(O)-, -C(O)NR<sup>58</sup>-, -SO<sub>2</sub>NR<sup>59</sup>-, -NR<sup>60</sup>SO<sub>2</sub>- or -NR<sup>61</sup>- (wherein R<sup>57</sup>, R<sup>58</sup>, R<sup>59</sup>, R<sup>60</sup> and R<sup>61</sup> each independently represents hydrogen,  $C_{1-3}$ alkyl or  $C_{1-3}$ alkoxy $C_{2-3}$ alkyl), and  $R^{56}$  is selected from one of the following twenty-two groups:

- 1) hydrogen, oxiranylc<sub>1-4</sub>alkyl or C<sub>1-5</sub>alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, chloro, bromo and amino;
  - 2) C<sub>1-5</sub>alkylX<sup>11</sup>C(O)R<sup>62</sup> (wherein X<sup>11</sup> represents -O- or -NR<sup>63</sup>- (in which R<sup>63</sup> represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>62</sup> represents C<sub>1-3</sub>alkyl, -NR<sup>64</sup>R<sup>65</sup> or -OR<sup>66</sup> (wherein R<sup>64</sup>, R<sup>65</sup> and R<sup>66</sup> which may be the same or different each represents hydrogen, C<sub>1-5</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl));
  - 3) C<sub>1-5</sub>alkylX<sup>12</sup>R<sup>67</sup> (wherein X<sup>12</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -OC(O)-, -NR<sup>68</sup>C(O)-, -C(O)NR<sup>69</sup>-, -SO<sub>2</sub>NR<sup>70</sup>-, -NR<sup>71</sup>SO<sub>2</sub>- or -NR<sup>72</sup>- (wherein R<sup>68</sup>, R<sup>69</sup>, R<sup>70</sup>, R<sup>71</sup> and R<sup>72</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>67</sup> represents hydrogen, C<sub>1-3</sub>alkyl, cyclopentyl, cyclohexyl or a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C<sub>1-3</sub>alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C<sub>1-4</sub>alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cyanooalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>aminoalkyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl);

$\text{C}_1\text{-alkoxy}$ ,  $\text{di}(\text{C}_{1-4}\text{alkyl})\text{aminoC}_{1-4}\text{alkoxy}$  and a group  $\text{(-O-)}_f(\text{C}_{1-4}\text{alkyl})_g\text{ringD}$  (wherein  $f$  is 0 or 1,  $g$  is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from  $\text{C}_{1-4}\text{alkyl}$ ));

4)  $\text{C}_{1-5}\text{salkylX}^{13}\text{C}_{1-5}\text{salkylX}^{14}\text{R}^{73}$  (wherein  $X^{13}$  and  $X^{14}$  which may be the same or different are each -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>74</sup>C(O)-, -C(O)NR<sup>75</sup>-, -SO<sub>2</sub>NR<sup>76</sup>-, -NR<sup>77</sup>SO<sub>2</sub>- or -NR<sup>78</sup>- (wherein R<sup>74</sup>, R<sup>75</sup>, R<sup>76</sup>, R<sup>77</sup> and R<sup>78</sup> each independently represents hydrogen,  $\text{C}_{1-3}\text{alkyl}$  or  $\text{C}_{1-3}\text{alkoxyC}_{2-3}\text{alkyl}$ ) and R<sup>73</sup> represents hydrogen,  $\text{C}_{1-3}\text{alkyl}$  or  $\text{C}_{1-3}\text{alkoxyC}_{2-3}\text{alkyl}$ );

5)  $\text{R}^{79}$  (wherein R<sup>79</sup> is a 4-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano,  $\text{C}_{1-4}\text{cyanoalkyl}$ ,  $\text{C}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{hydroxyalkyl}$ ,  $\text{C}_{1-4}\text{alkoxy}$ ,  $\text{C}_{1-4}\text{alkoxyC}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkylsulphonylC}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkoxycarbonyl}$ ,  $\text{C}_{1-4}\text{aminoalkyl}$ ,  $\text{C}_{1-4}\text{alkylamino}$ ,  $\text{di}(\text{C}_{1-4}\text{alkyl})\text{amino}$ ,  $\text{C}_{1-4}\text{alkylaminoC}_{1-4}\text{alkyl}$ ,  $\text{di}(\text{C}_{1-4}\text{alkyl})\text{aminoC}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkylaminoC}_{1-4}\text{alkoxy}$ ,  $\text{di}(\text{C}_{1-4}\text{alkyl})\text{aminoC}_{1-4}\text{alkoxy}$  and a group  $\text{(-O-)}_f(\text{C}_{1-4}\text{alkyl})_g\text{ringD}$  (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from  $\text{C}_{1-4}\text{alkyl}$ ));

6)  $\text{C}_{1-5}\text{salkylR}^{79}$  (wherein R<sup>79</sup> is as defined hereinbefore);

7)  $\text{C}_{2-5}\text{alkenylR}^{79}$  (wherein R<sup>79</sup> is as defined hereinbefore);

8)  $\text{C}_{2-5}\text{alkynylR}^{79}$  (wherein R<sup>79</sup> is as defined hereinbefore);

9)  $\text{R}^{80}$  (wherein R<sup>80</sup> represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents selected from hydroxy, halogeno, amino,  $\text{C}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkoxy}$ ,  $\text{C}_{1-4}\text{hydroxyalkyl}$ ,  $\text{C}_{1-4}\text{aminoalkyl}$ ,  $\text{C}_{1-4}\text{alkylamino}$ ,  $\text{C}_{1-4}\text{hydroxyalkoxy}$ , carboxy, trifluoromethyl, cyano, -C(O)NR<sup>81</sup>R<sup>82</sup>, -NR<sup>83</sup>C(O)R<sup>84</sup> (wherein R<sup>81</sup>, R<sup>82</sup>, R<sup>83</sup> and R<sup>84</sup>, which may be the same or different, each represents hydrogen,  $\text{C}_{1-4}\text{alkyl}$  or  $\text{C}_{1-3}\text{alkoxyC}_{2-3}\text{alkyl}$ ) and a group  $\text{(-O-)}_f(\text{C}_{1-4}\text{alkyl})_g\text{ringD}$  (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated

heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl));

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- 10) C<sub>1-5</sub>alkylR<sup>80</sup> (wherein R<sup>80</sup> is as defined hereinbefore);
  - 11) C<sub>2-5</sub>alkenylR<sup>80</sup> (wherein R<sup>80</sup> is as defined hereinbefore);
  - 12) C<sub>2-5</sub>alkynylR<sup>80</sup> (wherein R<sup>80</sup> is as defined hereinbefore);
  - 13) C<sub>1-5</sub>alkylX<sup>15</sup>R<sup>80</sup> (wherein X<sup>15</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>85</sup>C(O)-, -C(O)NR<sup>86</sup>-, -SO<sub>2</sub>NR<sup>87</sup>-, -NR<sup>88</sup>SO<sub>2</sub>- or -NR<sup>89</sup>- (wherein R<sup>85</sup>, R<sup>86</sup>, R<sup>87</sup>, R<sup>88</sup> and R<sup>89</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>80</sup> is as defined hereinbefore);
  - 14) C<sub>2-5</sub>alkenylX<sup>16</sup>R<sup>80</sup> (wherein X<sup>16</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>90</sup>C(O)-, -C(O)NR<sup>91</sup>-, -SO<sub>2</sub>NR<sup>92</sup>-, -NR<sup>93</sup>SO<sub>2</sub>- or -NR<sup>94</sup>- (wherein R<sup>90</sup>, R<sup>91</sup>, R<sup>92</sup>, R<sup>93</sup> and R<sup>94</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>80</sup> is as defined hereinbefore);
  - 15) C<sub>2-5</sub>alkynylX<sup>17</sup>R<sup>80</sup> (wherein X<sup>17</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>95</sup>C(O)-, -C(O)NR<sup>96</sup>-, -SO<sub>2</sub>NR<sup>97</sup>-, -NR<sup>98</sup>SO<sub>2</sub>- or -NR<sup>99</sup>- (wherein R<sup>95</sup>, R<sup>96</sup>, R<sup>97</sup>, R<sup>98</sup> and R<sup>99</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>80</sup> is as defined hereinbefore);
  - 16) C<sub>1-4</sub>alkylX<sup>18</sup>C<sub>1-4</sub>alkylR<sup>80</sup> (wherein X<sup>18</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>100</sup>C(O)-, -C(O)NR<sup>101</sup>-, -SO<sub>2</sub>NR<sup>102</sup>-, -NR<sup>103</sup>SO<sub>2</sub>- or -NR<sup>104</sup>- (wherein R<sup>100</sup>, R<sup>101</sup>, R<sup>102</sup>, R<sup>103</sup> and R<sup>104</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>80</sup> is as defined hereinbefore);
  - 17) C<sub>1-4</sub>alkylX<sup>18</sup>C<sub>1-4</sub>alkylR<sup>79</sup> (wherein X<sup>18</sup> and R<sup>79</sup> are as defined hereinbefore);
  - 18) C<sub>2-5</sub>alkenyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, amino, C<sub>1-4</sub>alkylamino, N,N-di(C<sub>1-4</sub>alkyl)amino, aminosulphonyl, N-C<sub>1-4</sub>alkylaminosulphonyl and N,N-di(C<sub>1-4</sub>alkyl)aminosulphonyl;
  - 19) C<sub>2-5</sub>alkynyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, amino, C<sub>1-4</sub>alkylamino, N,N-di(C<sub>1-4</sub>alkyl)amino, aminosulphonyl, N-C<sub>1-4</sub>alkylaminosulphonyl and N,N-di(C<sub>1-4</sub>alkyl)aminosulphonyl;
  - 20) C<sub>2-5</sub>alkenylX<sup>18</sup>C<sub>1-4</sub>alkylR<sup>79</sup> (wherein X<sup>18</sup> and R<sup>79</sup> are as defined hereinbefore);
  - 21) C<sub>2-5</sub>alkynylX<sup>18</sup>C<sub>1-4</sub>alkylR<sup>79</sup> (wherein X<sup>18</sup> and R<sup>79</sup> are as defined hereinbefore); and

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22)  $C_{1-4}alkylR^{105}(C_{1-4}alkyl)_x(X^{18})_yR^{106}$  (wherein  $X^{18}$  is as defined hereinbefore, x is 0 or 1, y is 0 or 1, and  $R^{105}$  and  $R^{106}$  are each independently selected from hydrogen,  $C_{1-3}alkyl$ , cyclopentyl, cyclohexyl and a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which  $C_{1-3}alkyl$  group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and  $C_{1-4}alkoxy$  and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano,  $C_{1-4}cyanoalkyl$ ,  $C_{1-4}alkyl$ ,  $C_{1-4}hydroxyalkyl$ ,  $C_{1-4}alkoxy$ ,  $C_{1-4}alkoxyC_{1-4}alkyl$ ,  $C_{1-4}alkylsulphonylC_{1-4}alkyl$ ,  $C_{1-4}alkoxycarbonyl$ ,  $C_{1-4}aminoalkyl$ ,  $C_{1-4}alkylamino$ ,  $di(C_{1-4}alkyl)amino$ ,  $C_{1-4}alkylaminoC_{1-4}alkyl$ ,  $di(C_{1-4}alkyl)aminoC_{1-4}alkyl$ ,  $C_{1-4}alkylaminoC_{1-4}alkoxy$ ,  $di(C_{1-4}alkyl)aminoC_{1-4}alkoxy$  and a group  $-(-O-)_f(C_{1-4}alkyl)_g$  ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from  $C_{1-4}alkyl$ ) with the proviso that  $R^{105}$  cannot be hydrogen);  
and additionally wherein any  $C_{1-5}alkyl$ ,  $C_{2-5}alkenyl$  or  $C_{2-5}salkynyl$  group in  $R^{56}X^{10}$  may bear one or more substituents selected from hydroxy, halogeno and amino);  
or a salt thereof, or a prodrug thereof for example an ester or an amide, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals such as humans.

\* \* \* \* \*

Please replace the paragraph on page 15, extending from line 24 to line 32 with the following amended paragraph:

A3  
Advantageously  $R^{105}$  and  $R^{106}$  are each independently a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano,  $C_{1-3}cyanoalkyl$ ,  $C_{1-3}alkyl$ ,  $C_{1-3}hydroxyalkyl$ ,  $C_{1-3}alkoxy$ ,  $C_{1-2}alkoxyC_{1-3}alkyl$ ,  $C_{1-2}alkylsulphonylC_{1-3}alkyl$ ,  $C_{1-3}alkoxycarbonyl$ ,  $C_{1-3}alkylamino$ ,  $di(C_{1-3}alkyl)amino$ ,  $C_{1-3}alkylaminoC_{1-3}alkyl$ ,  $di(C_{1-3}alkyl)aminoC_{1-3}alkyl$ ,  $C_{1-3}alkylaminoC_{1-3}alkoxy$ ,  $di(C_{1-3}alkyl)aminoC_{1-3}alkoxy$  and a group  $-(-O-)_f(C_{1-3}alkyl)_g$  ringD (wherein f is 0 or 1, g is 0 or 1)

*f3* and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-3</sub>alkyl).

\* \* \* \* \*

Please replace the paragraph extending from page 20, line 30 to page 21, line 5 with the following amended paragraph:

*f4* Advantageously R<sup>54</sup> and R<sup>55</sup> are each independently a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-3</sub>cyanoalkyl, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>hydroxyalkyl, C<sub>1-3</sub>alkoxy, C<sub>1-2</sub>alkoxyC<sub>1-3</sub>alkyl, C<sub>1-2</sub>alkylsulphonylC<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxycarbonyl and a group -(-O-)<sub>f</sub>(C<sub>1-3</sub>alkyl)<sub>g</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-3</sub>alkyl).

\* \* \* \* \*

Please replace the paragraphs extending from page 22, line 7 to page 23, line 8 with the following amended paragraphs:

*AS* 3) C<sub>2-4</sub>alkylX<sup>3</sup>R<sup>16</sup> (wherein X<sup>3</sup> is as hereinbefore defined and R<sup>16</sup> represents hydrogen, C<sub>1-3</sub>alkyl, cyclopentyl, cyclohexyl or a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C<sub>1-3</sub>alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C<sub>1-3</sub>alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cyanoalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkoxy, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkoxy and a group -

(-O-)<sub>f</sub>(C<sub>1-4</sub>alkyl)<sub>g</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl));

4) C<sub>2-3</sub>alkylX<sup>4</sup>C<sub>2-3</sub>alkylX<sup>5</sup>R<sup>22</sup> (wherein X<sup>4</sup> and X<sup>5</sup> are as hereinbefore defined and R<sup>22</sup> represents hydrogen or C<sub>1-3</sub>alkyl);

5) R<sup>28</sup> (wherein R<sup>28</sup> is as defined hereinbefore);

6) C<sub>1-5</sub>alkylR<sup>107</sup> (wherein R<sup>107</sup> is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C<sub>1-5</sub>alkyl through a carbon atom and which heterocyclic group may bear 1 or 2 substituents

*AS*  
selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cyanoalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkoxy, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkoxy and a group -(-O-)<sub>f</sub>(C<sub>1-4</sub>alkyl)<sub>g</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl)) or C<sub>2-5</sub>alkylR<sup>108</sup> (wherein R<sup>108</sup> is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, of which one is N and the other may be selected independently from O, S and N, which heterocyclic group is linked to C<sub>2-5</sub>alkyl through a nitrogen atom and which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cyanoalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkoxy, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkoxy and a group -(-O-)<sub>f</sub>(C<sub>1-4</sub>alkyl)<sub>g</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl));

\* \* \* \* \*

Please replace the paragraph extending from page 28, line 12 to page 30, line 21 with the following amended paragraph:

More preferably R<sup>2</sup> represents hydroxy, C<sub>1-3</sub>alkyl, amino or R<sup>5</sup>X<sup>1</sup>- [wherein X<sup>1</sup> is as hereinbefore defined and R<sup>5</sup> represents methyl, ethyl, benzyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2-hydroxyethyl, 3-hydroxypropyl, 2-methoxyethyl, 3-methoxypropyl, 2-(methylsulphanyl)ethyl, 2-(methylsulphonyl)ethyl, 2-(ethylsulphanyl)ethyl, 2-(ethylsulphonyl)ethyl, 2-(N,N-dimethylsulphamoyl)ethyl, 2-(N-methylsulphamoyl)ethyl, 2-sulphamoylethyl, 2-(methylamino)ethyl, 3-(methylamino)propyl, 2-(ethylamino)ethyl, 3-(ethylamino)propyl, 2-(N,N-dimethylamino)ethyl, 3-(N,N-dimethylamino)propyl, 2-(N,N-diethylamino)ethyl, 3-(N,N-diethylamino)propyl, 2-(N-methyl-N-methylsulphonylamino)ethyl, 3-(N-methyl-N-methylsulphonylamino)propyl, 2-morpholinoethyl, 3-morpholinopropyl, 2-piperidinoethyl, 3-piperidinopropyl, 2-(methylpiperidino)ethyl, 3-(methylpiperidino)propyl, 2-(ethylpiperidino)ethyl, 3-(ethylpiperidino)propyl, 2-((2-methoxyethyl)piperidino)ethyl, 3-((2-methoxyethyl)piperidino)propyl, 2-((2-methylsulphonyl)ethyl)piperidino)ethyl, 3-((2-methylsulphonyl)ethyl)piperidino)propyl, piperidin-3-ylmethyl, piperidin-4-ylmethyl, 2-(piperidin-3-yl)ethyl, 2-(piperidin-4-yl)ethyl, 3-(piperidin-3-yl)propyl, 3-(piperidin-4-yl)propyl, 2-(piperidin-2-yl)ethyl, 3-(piperidin-2-yl)propyl, (1-methylpiperidin-3-yl)methyl, (1-methylpiperidin-4-yl)methyl, (1-cyanomethylpiperidin-3-yl)methyl, (1-cyanomethylpiperidin-4-yl)methyl, 2-(methylpiperidin-3-yl)ethyl, 2-(methylpiperidin-4-yl)ethyl, 2-(1-cyanomethylpiperidin-3-yl)ethyl, 2-(1-cyanomethylpiperidin-4-yl)ethyl, 3-(methylpiperidin-3-yl)propyl, 3-(methylpiperidin-4-yl)propyl, 3-(1-cyanomethylpiperidin-3-yl)propyl, 3-(1-cyanomethylpiperidin-4-yl)propyl, 2-(ethylpiperidin-3-yl)ethyl, 2-(ethylpiperidin-4-yl)ethyl, ((2-methoxyethyl)piperidin-3-yl)methyl, ((2-methoxyethyl)piperidin-4-yl)methyl, 2-((2-methoxyethyl)piperidin-3-yl)ethyl, 2-((2-methoxyethyl)piperidin-4-yl)ethyl, 3-((2-methoxyethyl)piperidin-3-yl)propyl, 3-((2-methoxyethyl)piperidin-4-yl)propyl, (1-(2-methylsulphonylethyl)piperidin-4-yl)methyl, 2-((2-methylsulphonylethyl)piperidin-3-yl)ethyl, 2-((2-methylsulphonylethyl)piperidin-4-yl)ethyl, 3-((2-methylsulphonylethyl)piperidin-3-yl)propyl, 3-((2-methylsulphonylethyl)piperidin-4-yl)propyl, 1-isopropylpiperidin-2-

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ylmethyl, 1-isopropylpiperidin-3-ylmethyl, 1-isopropylpiperidin-4-ylmethyl, 2-(1-isopropylpiperidin-2-yl)ethyl, 2-(1-isopropylpiperidin-3-yl)ethyl, 2-(1-isopropylpiperidin-4-yl)ethyl, 3-(1-isopropylpiperidin-2-yl)propyl, 3-(1-isopropylpiperidin-3-yl)propyl, 3-(1-isopropylpiperidin-4-yl)propyl, 2-(piperidin-4-yloxy)ethyl, 3-(piperidin-4-yloxy)propyl, 2-(1-(cyanomethyl)piperidin-4-yloxy)ethyl, 3-(1-(cyanomethyl)piperidin-4-yloxy)propyl, 2-(1-(2-cyanoethyl)piperidin-4-yloxy)ethyl, 3-(1-(2-cyanoethyl)piperidin-4-yloxy)propyl, 2-(piperazin-1-yl)ethyl, 3-(piperazin-1-yl)propyl, (pyrrolidin-2-yl)methyl, 2-(pyrrolidin-1-yl)ethyl, 3-(pyrrolidin-1-yl)propyl, (2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, 5(R)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, (5S)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, (1,3-dioxolan-2-yl)methyl, 2-(1,3-dioxolan-2-yl)ethyl, 2-(2-methoxyethylamino)ethyl, 2-(N-(2-methoxyethyl)-N-methylamino)ethyl, 2-(hydroxyethylamino)ethyl, 3-(2-methoxyethylamino)propyl, 3-(N-(2-methoxyethyl)-N-methylamino)propyl, 3-(2-hydroxyethylamino)propyl, 2-methylthiazol-4-ylmethyl, 2-acetamidothiazol-4-ylmethyl, 1-methylimidazol-2-ylmethyl, 2-(imidazol-1-yl)ethyl, 2-(2-methylimidazol-1-yl)ethyl, 2-(2-ethylimidazol-1-yl)ethyl, 3-(2-methylimidazol-1-yl)propyl, 3-(2-ethylimidazol-1-yl)propyl, 2-(1,2,3-triazol-1-yl)ethyl, 2-(1,2,3-triazol-2-yl)ethyl, 2-(1,2,4-triazol-1-yl)ethyl, 2-(1,2,4-triazol-4-yl)ethyl, 4-pyridylmethyl, 2-(4-pyridyl)ethyl, 3-(4-pyridyl)propyl, 2-(4-pyridyloxy)ethyl, 2-(4-pyridylamino)ethyl, 2-(4-oxo-1,4-dihydro-1-pyridyl)ethyl, 2-(2-oxo-imidazolidin-1-yl)ethyl, 3-(2-oxo-imidazolidin-1-yl)propyl, 2-thiomorpholinoethyl, 3-thiomorpholinopropyl, 2-(1,1-dioxothiomorpholino)ethyl, 3-(1,1-dioxothiomorpholino)propyl, 2-(2-methoxyethoxy)ethyl, 2-(4-methylpiperazin-1-yl)ethyl, 3-(4-methylpiperazin-1-yl)propyl, 3-(methylsulphanyl)propyl, 3-(methylsulphonyl)propyl, 3-(ethylsulphanyl)propyl, 3-(ethylsulphonyl)propyl, 2-(5-methyl-1,2,4-triazol-1-yl)ethyl, morpholino, 2-((N-(1-methylimidazol-4-ylsulphonyl)-N-methyl)amino)ethyl, 2-((N-(3-morpholinopropylsulphonyl)-N-methyl)amino)ethyl, 2-((N-methyl-N-4-pyridyl)amino)ethyl, 3-(4-oxidomorpholino)propyl, 2-(2-(4-methylpiperazin-1-yl)ethoxy)ethyl, 3-(2-(4-methylpiperazin-1-yl)ethoxy)propyl, 2-(2-morpholinoethoxy)ethyl, 3-(2-morpholinoethoxy)propyl, 2-(tetrahydropyran-4-yloxy)ethyl, 3-(tetrahydropyran-4-yloxy)propyl, 2-((2-(pyrrolidin-1-yl)ethyl)carbamoyl)vinyl, 3-((2-(pyrrolidin-1-yl)ethyl)carbamoyl)prop-2-en-1-yl, 1-(2-pyrrolidinylethyl)piperidin-4-ylmethyl, 1-(3-

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pyrrolidinylpropyl)piperidin-4-ylmethyl, 1-(2-piperidinylethyl)piperidin-4-ylmethyl, 1-(3-piperidinylpropyl)piperidin-4-ylmethyl, 1-(2-morpholinoethyl)piperidin-4-ylmethyl, 1-(3-morpholinopropyl)piperidin-4-ylmethyl, 1-(2-thiomorpholinoethyl)piperidin-4-ylmethyl, 1-(3-thiomorpholinopropyl)piperidin-4-ylmethyl, 1-(2-azetidinylethyl)piperidin-4-ylmethyl,  
[or] 1-(3-azetidinylpropyl)piperidin-4-ylmethyl, 3-morpholino-2-hydroxypropyl, (2R)-3-morpholino-2-hydroxypropyl, (2S)-3-morpholino-2-hydroxypropyl, 3-piperidino-2-hydroxypropyl, (2R)-3-piperidino-2-hydroxypropyl, (2S)-3-piperidino-2-hydroxypropyl, 3-pyrrolidin-1-yl-2-hydroxypropyl, (2R)-3-pyrrolidin-1-yl-2-hydroxypropyl, (2S)-3-pyrrolidin-1-yl-2-hydroxypropyl, 3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, (2R)-3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, (2S)-3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, 3-(N,N-diethylamino)-2-hydroxypropyl, (2R)-3-(N,N-diethylamino)-2-hydroxypropyl, (2S)-3-(N,N-diethylamino)-2-hydroxypropyl, 3-(isopropylamino)-2-hydroxypropyl, (2R)-3-(isopropylamino)-2-hydroxypropyl, (2S)-3-(isopropylamino)-2-hydroxypropyl, 3-(N,N-diisopropylamino)-2-hydroxypropyl, (2R)-3-(N,N-diisopropylamino)-2-hydroxypropyl or (2S)-3-(N,N-diisopropylamino)-2-hydroxypropyl].

\* \* \* \* \*

Please replace the paragraph extending from page 30, line 22 to page 32, line 30 with the following amended paragraph:

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Particularly R<sup>2</sup> represents C<sub>1-3</sub>alkyl, amino or R<sup>5</sup>X<sup>1</sup>- [wherein X<sup>1</sup> is as hereinbefore defined and R<sup>5</sup> represents ethyl, benzyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2-hydroxyethyl, 3-hydroxypropyl, 2-methoxyethyl, 3-methoxypropyl, 2-(methylsulphinyl)ethyl, 2-(methylsulphonyl)ethyl, 2-(ethylsulphinyl)ethyl, 2-(ethylsulphonyl)ethyl, 2-(N,N-dimethylsulphamoyl)ethyl, 2-(N-methylsulphamoyl)ethyl, 2-sulphamoyleethyl, 2-(methylamino)ethyl, 3-(methylamino)propyl, 2-(ethylamino)ethyl, 3-(ethylamino)propyl, 2-(N,N-dimethylamino)ethyl, 3-(N,N-dimethylamino)propyl, 2-(N,N-diethylamino)ethyl, 3-(N,N-diethylamino)propyl, 2-(N-methyl-N-methylsulphonylamino)ethyl, 3-(N-methyl-N-methylsulphonylamino)propyl, 2-morpholinoethyl, 3-morpholinopropyl, 2-piperidinoethyl, 3-piperidinopropyl, 2-(methylpiperidino)ethyl, 3-(methylpiperidino)propyl, 2-

(ethylpiperidino)ethyl, 3-(ethylpiperidino)propyl, 2-((2-methoxyethyl)piperidino)ethyl, 3-((2-methoxyethyl)piperidino)propyl, 2-((2-methylsulphonyl)ethylpiperidino)ethyl, 3-((2-methylsulphonyl)ethylpiperidino)propyl, piperidin-3-ylmethyl, piperidin-4-ylmethyl, 2-(piperidin-3-yl)ethyl, 2-(piperidin-4-yl)ethyl, 3-(piperidin-3-yl)propyl, 3-(piperidin-4-yl)propyl, 2-(piperidin-2-yl)ethyl, 3-(piperidin-2-yl)propyl, (1-methylpiperidin-3-yl)methyl, (1-methylpiperidin-4-yl)methyl, (1-cyanomethylpiperidin-3-yl)methyl, (1-cyanomethylpiperidin-4-yl)methyl, 2-(methylpiperidin-3-yl)ethyl, 2-(methylpiperidin-4-yl)ethyl, 2-(1-cyanomethylpiperidin-3-yl)ethyl, 2-(1-cyanomethylpiperidin-4-yl)ethyl, 3-(methylpiperidin-3-yl)propyl, 3-(methylpiperidin-4-yl)propyl, 3-(1-cyanomethylpiperidin-3-yl)propyl, 3-(1-cyanomethylpiperidin-4-yl)propyl, 2-(ethylpiperidin-3-yl)ethyl, 2-(ethylpiperidin-4-yl)ethyl, 3-(ethylpiperidin-3-yl)propyl, 3-(ethylpiperidin-4-yl)propyl, ((2-methoxyethyl)piperidin-3-yl)methyl, ((2-methoxyethyl)piperidin-4-yl)methyl, 2-((2-methoxyethyl)piperidin-3-yl)ethyl, 2-((2-methoxyethyl)piperidin-4-yl)ethyl, 3-((2-methoxyethyl)piperidin-3-yl)propyl, 3-((2-methoxyethyl)piperidin-4-yl)propyl, (1-(2-methylsulphonylethyl)piperidin-3-yl)methyl, (1-(2-methylsulphonylethyl)piperidin-4-yl)methyl, 2-((2-methylsulphonylethyl)piperidin-3-yl)ethyl, 2-((2-methylsulphonylethyl)piperidin-4-yl)ethyl, 3-((2-methylsulphonylethyl)piperidin-3-yl)propyl, 3-((2-methylsulphonylethyl)piperidin-4-yl)propyl, 1-isopropylpiperidin-2-ylmethyl, 1-isopropylpiperidin-3-ylmethyl, 1-isopropylpiperidin-4-ylmethyl, 2-(1-isopropylpiperidin-2-yl)ethyl, 2-(1-isopropylpiperidin-3-yl)ethyl, 2-(1-isopropylpiperidin-4-yl)ethyl, 3-(1-isopropylpiperidin-2-yl)propyl, 3-(1-isopropylpiperidin-3-yl)propyl, 3-(1-isopropylpiperidin-4-yl)propyl, 2-(piperidin-4-yloxy)ethyl, 3-(piperidin-4-yloxy)propyl, 2-(1-(cyanomethyl)piperidin-4-yloxy)ethyl, 3-(1-(cyanomethyl)piperidin-4-yloxy)propyl, 2-(1-(2-cyanoethyl)piperidin-4-yloxy)ethyl, 3-(1-(2-cyanoethyl)piperidin-4-yloxy)propyl, 2-(piperazin-1-yl)ethyl, 3-(piperazin-1-yl)propyl, (pyrrolidin-2-yl)methyl, 2-(pyrrolidin-1-yl)ethyl, 3-(pyrrolidin-1-yl)propyl, (2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, 5(R)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, (5S)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, (1,3-dioxolan-2-yl)methyl, 2-(1,3-dioxolan-2-yl)ethyl, 2-(2-methoxyethylamino)ethyl, 2-(N-(2-methoxyethyl)-N-methylamino)ethyl, 2-(2-hydroxyethylamino)ethyl, 3-(2-methoxyethylamino)propyl, 3-(N-(2-methoxyethyl)-N-methylamino)propyl, 3-(2-

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hydroxyethylamino)propyl, 2-methylthiazol-4-ylmethyl, 2-acetamidothiazol-4-ylmethyl, 1-methylimidazol-2-ylmethyl, 2-(imidazol-1-yl)ethyl, 2-(2-methylimidazol-1-yl)ethyl, 2-(2-ethylimidazol-1-yl)ethyl, 3-(2-methylimidazol-1-yl)propyl, 3-(2-ethylimidazol-1-yl)propyl, 2-(1,2,3-triazol-1-yl)ethyl, 2-(1,2,3-triazol-2-yl)ethyl, 2-(1,2,4-triazol-1-yl)ethyl, 2-(1,2,4-triazol-4-yl)ethyl, 4-pyridylmethyl, 2-(4-pyridyl)ethyl, 3-(4-pyridyl)propyl, 2-(4-pyridyloxy)ethyl, 2-(4-pyridylamino)ethyl, 2-(4-oxo-1,4-dihydro-1-pyridyl)ethyl, 2-(2-oxo-imidazolidin-1-yl)ethyl, 3-(2-oxo-imidazolidin-1-yl)propyl, 2-thiomorpholinoethyl, 3-thiomorpholinopropyl, 2-(1,1-dioxothiomorpholino)ethyl, 3-(1,1-dioxothiomorpholino)propyl, 2-(2-methoxyethoxy)ethyl, 2-(4-methylpiperazin-1-yl)ethyl, 3-(4-methylpiperazin-1-yl)propyl, 3-(methylsulphanyl)propyl, 3-(methylsulphonyl)propyl, 3-(ethylsulphanyl)propyl, 3-(ethylsulphonyl)propyl, 2-(5-methyl-1,2,4-triazol-1-yl)ethyl, morpholino, 2-((N-(1-methylimidazol-4-ylsulphonyl)-N-methyl)amino)ethyl, 2-((N-(3-morpholinopropylsulphonyl)-N-methyl)amino)ethyl, 2-((N-methyl-N-4-pyridyl)amino)ethyl, 3-(4-oxidomorpholino)propyl, 2-(2-(4-methylpiperazin-1-yl)ethoxy)ethyl, 3-(2-(4-methylpiperazin-1-yl)ethoxy)propyl, 2-(2-morpholinoethoxy)ethyl, 3-(2-morpholinoethoxy)propyl, 2-(tetrahydropyran-4-yloxy)ethyl, 3-(tetrahydropyran-4-yloxy)propyl, 2-((2-(pyrrolidin-1-yl)ethyl)carbamoyl)vinyl, 3-((2-(pyrrolidin-1-yl)ethyl)carbamoyl)prop-2-en-1-yl, 1-(2-pyrrolidinylethyl)piperidin-4-ylmethyl, 1-(3-pyrrolidinylpropyl)piperidin-4-ylmethyl, 1-(2-piperidinylethyl)piperidin-4-ylmethyl, 1-(3-piperidinylpropyl)piperidin-4-ylmethyl, 1-(2-morpholinoethyl)piperidin-4-ylmethyl, 1-(3-morpholinopropyl)piperidin-4-ylmethyl, 1-(2-thiomorpholinoethyl)piperidin-4-ylmethyl, 1-(3-thiomorpholinopropyl)piperidin-4-ylmethyl, 1-(2-azetidinylethyl)piperidin-4-ylmethyl, 1-(3-azetidinylpropyl)piperidin-4-ylmethyl, 3-morpholino-2-hydroxypropyl, (2R)-3-morpholino-2-hydroxypropyl, (2S)-3-morpholino-2-hydroxypropyl, 3-piperidino-2-hydroxypropyl, (2R)-3-piperidino-2-hydroxypropyl, (2S)-3-piperidino-2-hydroxypropyl, 3-pyrrolidin-1-yl-2-hydroxypropyl, (2R)-3-pyrrolidin-1-yl-2-hydroxypropyl, (2S)-3-pyrrolidin-1-yl-2-hydroxypropyl, 3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, (2R)-3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, (2S)-3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, 3-(N,N-diethylamino)-2-hydroxypropyl, (2R)-3-(N,N-diethylamino)-2-hydroxypropyl, 3-(isopropylamino)-2-hydroxypropyl, (2R)-3-(isopropylamino)-2-hydroxypropyl, (2S)-3-(isopropylamino)-2-hydroxypropyl, 3-(N,N-

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diisopropylamino)-2-hydroxypropyl, (2R)-3-(N,N-diisopropylamino)-2-hydroxypropyl or (2S)-3-(N,N-diisopropylamino)-2-hydroxypropyl].

\* \* \* \* \*

Please replace the paragraph extending from page 32, line 31 to page 35, line 3 with the following amended paragraph:

More particularly R<sup>2</sup> represents C<sub>1-3</sub>alkyl, amino or R<sup>5</sup>X<sup>1</sup>- [wherein X<sup>1</sup> is as hereinbefore defined and R<sup>5</sup> represents ethyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2-hydroxyethyl, 3-hydroxypropyl, 2-methoxyethyl, 3-methoxypropyl, 2-(methylsulphinyl)ethyl, 2-(methylsulphonyl)ethyl, 2-(ethylsulphinyl)ethyl, 2-(ethylsulphonyl)ethyl, 2-(N,N-dimethylsulphamoyl)ethyl, 2-(N-methylsulphamoyl)ethyl, 2-sulphamoylethyl, 2-(methylamino)ethyl, 3-(methylamino)propyl, 2-(ethylamino)ethyl, 3-(ethylamino)propyl, 2-(N,N-dimethylamino)ethyl, 3-(N,N-dimethylamino)propyl, 2-(N,N-diethylamino)ethyl, 3-(N,N-diethylamino)propyl, 2-(N-methyl-N-methylsulphonylamino)ethyl, 3-(N-methyl-N-methylsulphonylamino)propyl, 2-morpholinoethyl, 3-morpholinopropyl, 2-piperidinoethyl, 3-piperidinopropyl, 2-(methylpiperidino)ethyl, 3-(methylpiperidino)propyl, 2-(ethylpiperidino)ethyl, 3-(ethylpiperidino)propyl, 2-((2-methoxyethyl)piperidino)ethyl, 3-((2-methoxyethyl)piperidino)propyl, 2-((2-methylsulphonyl)ethylpiperidino)ethyl, 3-((2-methylsulphonyl)ethylpiperidino)propyl, piperidin-3-ylmethyl, piperidin-4-ylmethyl, 2-(piperidin-3-yl)ethyl, 2-(piperidin-4-yl)ethyl, 3-(piperidin-3-yl)propyl, 3-(piperidin-4-yl)propyl, 2-(piperidin-2-yl)ethyl, 3-(piperidin-2-yl)propyl, (1-methylpiperidin-3-yl)methyl, (1-methylpiperidin-4-yl)methyl, (1-cyanomethylpiperidin-3-yl)methyl, (1-cyanomethylpiperidin-4-yl)methyl, 2-(methylpiperidin-3-yl)ethyl, 2-(methylpiperidin-4-yl)ethyl, 2-(1-cyanomethylpiperidin-3-yl)ethyl, 2-(1-cyanomethylpiperidin-4-yl)ethyl, 3-(methylpiperidin-3-yl)propyl, 3-(methylpiperidin-4-yl)propyl, 3-(1-cyanomethylpiperidin-3-yl)propyl, 3-(1-cyanomethylpiperidin-4-yl)propyl, 2-(ethylpiperidin-3-yl)ethyl, 2-(ethylpiperidin-4-yl)ethyl, ((2-methoxyethyl)piperidin-3-yl)methyl, ((2-methoxyethyl)piperidin-4-yl)methyl, 2-((2-methoxyethyl)piperidin-3-yl)ethyl, 2-((2-methoxyethyl)piperidin-4-yl)ethyl, 3-((2-

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methoxyethyl)piperidin-3-yl)propyl, 3-((2-methoxyethyl)piperidin-4-yl)propyl, (1-(2-methylsulphonylethyl)piperidin-3-yl)methyl, (1-(2-methylsulphonylethyl)piperidin-4-yl)methyl, 2-((2-methylsulphonylethyl)piperidin-3-yl)ethyl, 2-((2-methylsulphonylethyl)piperidin-4-yl)ethyl, 3-((2-methylsulphonylethyl)piperidin-3-yl)propyl, 3-((2-methylsulphonylethyl)piperidin-4-yl)propyl, 1-isopropylpiperidin-2-ylmethyl, 1-isopropylpiperidin-3-ylmethyl, 1-isopropylpiperidin-4-ylmethyl, 2-(1-isopropylpiperidin-2-yl)ethyl, 2-(1-isopropylpiperidin-3-yl)ethyl, 2-(1-isopropylpiperidin-4-yl)ethyl, 3-(1-isopropylpiperidin-2-yl)propyl, 3-(1-isopropylpiperidin-3-yl)propyl, 3-(1-isopropylpiperidin-4-yl)propyl, 2-(piperidin-4-yloxy)ethyl, 3-(piperidin-4-yloxy)propyl, 2-(1-(cyanomethyl)piperidin-4-yloxy)ethyl, 3-(1-(cyanomethyl)piperidin-4-yloxy)propyl, 2-(1-(2-cyanoethyl)piperidin-4-yloxy)ethyl, 3-(1-(2-cyanoethyl)piperidin-4-yloxy)propyl, 2-(piperazin-1-yl)ethyl, 3-(piperazin-1-yl)propyl, (pyrrolidin-2-yl)methyl, 2-(pyrrolidin-1-yl)ethyl, 3-(pyrrolidin-1-yl)propyl, (2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, 5(R)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, (5S)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methyl, (1,3-dioxolan-2-yl)methyl, 2-(1,3-dioxolan-2-yl)ethyl, 2-(2-methoxyethylamino)ethyl, 2-(N-(2-methoxyethyl)-N-methylamino)ethyl, 2-(2-hydroxyethylamino)ethyl, 3-(2-methoxyethylamino)propyl, 3-(N-(2-methoxyethyl)-N-methylamino)propyl, 3-(2-hydroxyethylamino)propyl, 2-(1,2,3-triazol-1-yl)ethyl, 2-(1,2,3-triazol-2-yl)ethyl, 2-(1,2,4-triazol-1-yl)ethyl, 2-(1,2,4-triazol-4-yl)ethyl, 4-pyridylmethyl, 2-(4-pyridyl)ethyl, 3-(4-pyridyl)propyl, 2-(4-pyridyloxy)ethyl, 2-(4-pyridylamino)ethyl, 2-(4-oxo-1,4-dihydro-1-pyridyl)ethyl, 2-(2-oxo-imidazolidin-1-yl)ethyl, 3-(2-oxo-imidazolidin-1-yl)propyl, 2-thiomorpholinoethyl, 3-thiomorpholinopropyl, 2-(1,1-dioxothiomorpholino)ethyl, 3-(1,1-dioxothiomorpholino)propyl, 2-(2-methoxyethoxy)ethyl, 2-(4-methylpiperazin-1-yl)ethyl, 3-(4-methylpiperazin-1-yl)propyl, 3-(methylsulphanyl)propyl, 3-(methylsulphonyl)propyl, 3-(ethylsulphanyl)propyl, 3-(ethylsulphonyl)propyl, 2-(5-methyl-1,2,4-triazol-1-yl)ethyl, morpholino, 2-((N-(3-morpholinopropylsulphonyl)-N-methyl)amino)ethyl, 2-((N-methyl-N-4-pyridyl)amino)ethyl, 3-(4-oxidomorpholino)propyl, 2-(2-(4-methylpiperazin-1-yl)ethoxy)ethyl, 3-(2-morpholinoethoxy)propyl, 2-(tetrahydropyran-4-yloxy)ethyl, 3-(tetrahydropyran-4-yloxy)propyl, 2-((2-(pyrrolidin-1-yl)ethyl)carbamoyl)vinyl, 3-((2-(pyrrolidin-1-

A8      yl)ethyl)carbamoyl)prop-2-en-1-yl, 1-(2-pyrrolidinylethyl)piperidin-4-ylmethyl, 1-(3-pyrrolidinylpropyl)piperidin-4-ylmethyl, 1-(2-piperidinylethyl)piperidin-4-ylmethyl, 1-(3-piperidinylpropyl)piperidin-4-ylmethyl, 1-(2-morpholinoethyl)piperidin-4-ylmethyl, 1-(3-morpholinopropyl)piperidin-4-ylmethyl, 1-(2-thiomorpholinoethyl)piperidin-4-ylmethyl, 1-(3-thiomorpholinopropyl)piperidin-4-ylmethyl, 1-(2-azetidinylethyl)piperidin-4-ylmethyl, 1-(3-azetidinylpropyl)piperidin-4-ylmethyl, 3-morpholino-2-hydroxypropyl, (2R)-3-morpholino-2-hydroxypropyl, (2S)-3-morpholino-2-hydroxypropyl, 3-piperidino-2-hydroxypropyl, (2R)-3-piperidino-2-hydroxypropyl, (2S)-3-piperidino-2-hydroxypropyl, 3-pyrrolidin-1-yl-2-hydroxypropyl, (2R)-3-pyrrolidin-1-yl-2-hydroxypropyl, (2S)-3-pyrrolidin-1-yl-2-hydroxypropyl, 3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, (2R)-3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, (2S)-3-(1-methylpiperazin-4-yl)-2-hydroxypropyl, 3-(N,N-diethylamino)-2-hydroxypropyl, (2R)-3-(N,N-diethylamino)-2-hydroxypropyl, (2S)-3-(N,N-diethylamino)-2-hydroxypropyl, 3-(isopropylamino)-2-hydroxypropyl, (2R)-3-(isopropylamino)-2-hydroxypropyl, (2S)-3-(isopropylamino)-2-hydroxypropyl, 3-(N,N-diisopropylamino)-2-hydroxypropyl, (2R)-3-(N,N-diisopropylamino)-2-hydroxypropyl or (2S)-3-(N,N-diisopropylamino)-2-hydroxypropyl].

\* \* \* \* \*

A9      Please replace the paragraph extending from page 35, line 4 to page 37, line 11 with the following amended paragraph:

In another aspect R<sup>2</sup> represents ethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, 2-hydroxyethoxy, 3-hydroxypropoxy, 2-methoxyethoxy, 3-methoxypropoxy, 2-(methylsulphonyl)ethoxy, 2-(methylsulphonyl)ethoxy, 2-(ethylsulphonyl)ethoxy, 2-(N,N-dimethylsulphamoyl)ethoxy, 2-(N-ethylsulphonyl)ethoxy, 2-sulphamoylethoxy, 2-(methylamino)ethoxy, 3-(methylamino)propoxy, 2-(ethylamino)ethoxy, 3-(ethylamino)propoxy, 2-(N,N-dimethylamino)ethoxy, 3-(N,N-dimethylamino)propoxy, 2-(N,N-diethylamino)ethoxy, 3-(N,N-diethylamino)propoxy, 2-(N-methyl-N-methylsulphonylamino)ethoxy, 3-(N-methyl-N-methylsulphonylamino)propoxy, 2-morpholinoethoxy, 3-morpholinopropoxy, 2-

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piperidinoethoxy, 3-piperidinopropoxy, 2-(methylpiperidino)ethoxy, 3-(methylpiperidino)propoxy, 2-(ethylpiperidino)ethoxy, 3-(ethylpiperidino)propoxy, 2-((2-methoxyethyl)piperidino)ethoxy, 3-((2-methoxyethyl)piperidino)propoxy, 2-((2-methylsulphonyl)ethylpiperidino)ethoxy, 3-((2-methylsulphonyl)ethylpiperidino)propoxy, piperidin-3-ylmethoxy, piperidin-4-ylmethoxy, 2-(piperidin-3-yl)ethoxy, 2-(piperidin-4-yl)ethoxy, 3-(piperidin-3-yl)propoxy, 3-(piperidin-4-yl)propoxy, 2-(piperidin-2-yl)ethoxy, 3-(piperidin-2-yl)propoxy, (1-methylpiperidin-3-yl)methoxy, (1-methylpiperidin-4-yl)methoxy, (1-cyanomethylpiperidin-3-yl)methoxy, (1-cyanomethylpiperidin-4-yl)methoxy, 2-(methylpiperidin-3-yl)ethoxy, 2-(methylpiperidin-4-yl)ethoxy, 2-(1-cyanomethylpiperidin-3-yl)ethoxy, 2-(1-cyanomethylpiperidin-4-yl)ethoxy, 3-(methylpiperidin-3-yl)propoxy, 3-(methylpiperidin-4-yl)propoxy, 3-(1-cyanomethylpiperidin-3-yl)propoxy, 3-(1-cyanomethylpiperidin-4-yl)propoxy, 2-(ethylpiperidin-3-yl)ethoxy, 2-(ethylpiperidin-4-yl)ethoxy, 3-(ethylpiperidin-3-yl)propoxy, 3-(ethylpiperidin-4-yl)propoxy, ((2-methoxyethyl)piperidin-3-yl)methoxy, ((2-methoxyethyl)piperidin-4-yl)methoxy, 2-((2-methoxyethyl)piperidin-3-yl)ethoxy, 2-((2-methoxyethyl)piperidin-4-yl)ethoxy, 3-((2-methoxyethyl)piperidin-3-yl)propoxy, 3-((2-methoxyethyl)piperidin-4-yl)propoxy, (1-(2-methylsulphonylethyl)piperidin-3-yl)methoxy, (1-(2-methylsulphonylethyl)piperidin-4-yl)methoxy, 2-((2-methylsulphonylethyl)piperidin-3-yl)ethoxy, 2-((2-methylsulphonylethyl)piperidin-4-yl)ethoxy, 3-((2-methylsulphonylethyl)piperidin-3-yl)propoxy, 3-((2-methylsulphonylethyl)piperidin-4-yl)propoxy, 1-isopropylpiperidin-2-ylmethoxy, 1-isopropylpiperidin-3-ylmethoxy, 1-isopropylpiperidin-4-ylmethoxy, 2-(1-isopropylpiperidin-2-yl)ethoxy, 2-(1-isopropylpiperidin-3-yl)ethoxy, 2-(1-isopropylpiperidin-4-yl)ethoxy, 3-(1-isopropylpiperidin-2-yl)propoxy, 3-(1-isopropylpiperidin-3-yl)propoxy, 3-(1-isopropylpiperidin-4-yl)propoxy, 2-(piperidin-4-yloxy)ethoxy, 3-(piperidin-4-yloxy)propoxy, 2-(1-(cyanomethyl)piperidin-4-yloxy)ethoxy, 3-(1-(cyanomethyl)piperidin-4-yloxy)propoxy, 2-(1-(2-cyanoethyl)piperidin-4-yloxy)ethoxy, 3-(1-(2-cyanoethyl)piperidin-4-yloxy)propoxy, 2-(piperazin-1-yl)ethoxy, 3-(piperazin-1-yl)propoxy, (pyrrolidin-2-yl)methoxy, 2-(pyrrolidin-1-yl)ethoxy, 3-(pyrrolidin-1-yl)propoxy, (2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methoxy, 5(R)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methoxy, (5S)-(2-oxo-tetrahydro-2H-pyrrolidin-5-yl)methoxy, (1,3-dioxolan-2-yl)methoxy, 2-(1,3-dioxolan-2-

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yl)ethoxy, 2-(2-methoxyethylamino)ethoxy, 2-(N-(2-methoxyethyl)-N-methylamino)ethoxy, 2-(2-hydroxyethylamino)ethoxy, 3-(2-methoxyethylamino)propoxy, 3-(N-(2-methoxyethyl)-N-methylamino)propoxy, 3-(2-hydroxyethylamino)propoxy, 2-(1,2,3-triazol-1-yl)ethoxy, 2-(1,2,3-triazol-2-yl)ethoxy, 2-(1,2,4-triazol-1-yl)ethoxy, 2-(1,2,4-triazol-4-yl)ethoxy, 4-pyridylmethoxy, 2-(4-pyridyl)ethoxy, 3-(4-pyridyl)propoxy, 2-(4-pyridyloxy)ethoxy, 2-(4-pyridylamino)ethoxy, 2-(4-oxo-1,4-dihydro-1-pyridyl)ethoxy, 2-(2-oxo-imidazolidin-1-yl)ethoxy, 3-(2-oxo-imidazolidin-1-yl)propoxy, 2-thiomorpholinoethoxy, 3-thiomorpholinopropoxy, 2-(1,1-dioxothiomorpholino)ethoxy, 3-(1,1-dioxothiomorpholino)propoxy, 2-(2-methoxyethoxy)ethoxy, 2-(4-methylpiperazin-1-yl)ethoxy, 3-(4-methylpiperazin-1-yl)propoxy, 3-(methylsulphinyl)propoxy, 3-(methylsulphonyl)propoxy, 3-(ethylsulphinyl)propoxy, 3-(ethylsulphonyl)propoxy, 2-(5-methyl-1,2,4-triazol-1-yl)ethoxy, 2-((N-(3-morpholinopropylsulphonyl)-N-methyl)amino)ethoxy, 2-((N-methyl-N-4-pyridyl)amino)ethoxy, 3-(4-oxidomorpholino)propoxy, 2-(2-(4-methylpiperazin-1-yl)ethoxy)ethoxy, 3-(2-(4-methylpiperazin-1-yl)ethoxy)propoxy, 2-(2-morpholinoethoxy)ethoxy, 3-(2-morpholinoethoxy)propoxy, 2-(tetrahydropyran-4-yloxy)ethoxy, 3-(tetrahydropyran-4-yloxy)propoxy, 2-((2-(pyrrolidin-1-yl)ethyl)carbamoyl)vinyl, 3-((2-(pyrrolidin-1-yl)ethyl)carbamoyl)prop-2-en-1-yloxy, 1-(2-pyrrolidinylethyl)piperidin-4-ylmethoxy, 1-(3-pyrrolidinylpropyl)piperidin-4-ylmethoxy, 1-(2-piperidinylethyl)piperidin-4-ylmethoxy, 1-(3-piperidinylpropyl)piperidin-4-ylmethoxy, 1-(2-morpholinoethyl)piperidin-4-ylmethoxy, 1-(3-morpholinopropyl)piperidin-4-ylmethoxy, 1-(2-thiomorpholinoethyl)piperidin-4-ylmethoxy, 1-(3-thiomorpholinopropyl)piperidin-4-ylmethoxy, 1-(2-azetidinylethyl)piperidin-4-ylmethoxy, 1-(3-azetidinylpropyl)piperidin-4-ylmethoxy, 3-morpholino-2-hydroxypropoxy, (2R)-3-morpholino-2-hydroxypropoxy, (2S)-3-morpholino-2-hydroxypropoxy, 3-piperidino-2-hydroxypropoxy, (2R)-3-piperidino-2-hydroxypropoxy, (2S)-3-piperidino-2-hydroxypropoxy, 3-pyrrolidin-1-yl-2-hydroxypropoxy, (2R)-3-pyrrolidin-1-yl-2-hydroxypropoxy, 3-(1-methylpiperazin-4-yl)-2-hydroxypropoxy, (2R)-3-(1-methylpiperazin-4-yl)-2-hydroxypropoxy, 3-(N,N-diethylamino)-2-hydroxypropoxy, (2R)-3-(N,N-diethylamino)-2-hydroxypropoxy, (2S)-3-(N,N-diethylamino)-2-hydroxypropoxy, (2S)-3-(N,N-diethylamino)-2-hydroxypropoxy,

A9 diethylamino)-2-hydroxypropoxy, 3-(isopropylamino)-2-hydroxypropoxy, (2R)-3-(isopropylamino)-2-hydroxypropoxy, (2S)-3-(isopropylamino)-2-hydroxypropoxy, 3-(N,N-diisopropylamino)-2-hydroxypropoxy, (2R)-3-(N,N-diisopropylamino)-2-hydroxypropoxy or (2S)-3-(N,N-diisopropylamino)-2-hydroxypropoxy.

\* \* \* \* \*

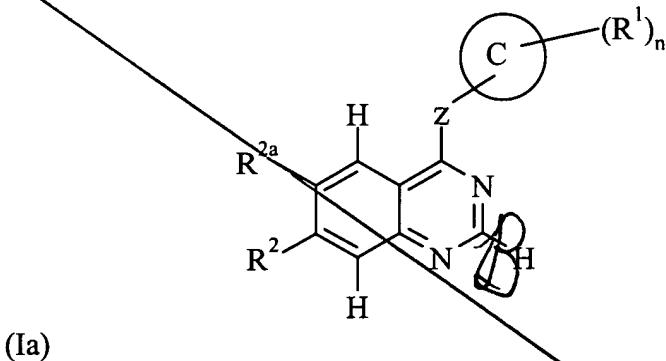
Please replace subparagraph numbered 12) at page 38, line 13, with the following new subparagraph:

A10 12) C<sub>1-5</sub>alkylX<sup>6</sup>R<sup>29</sup> (wherein X<sup>6</sup> and R<sup>29</sup> are as defined hereinbefore);

\* \* \* \* \*

Please replace the paragraph extending from page 47, line 26 to page 48, line 28 with the following amended paragraph:

In another aspect of the present invention there is provided the use of compounds of the formula Ia:



[wherein:

ring C, R<sup>1</sup>, R<sup>2</sup>, n and Z are as defined hereinbefore with the provisos that R<sup>2</sup> is not hydrogen and that Z is not CH<sub>2</sub> or a direct bond; and

R<sup>2a</sup> represents hydrogen, halogeno, C<sub>1-3</sub>alkyl, trifluoromethyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkylsulphanyl, -NR<sup>3a</sup>R<sup>4a</sup> (wherein R<sup>3a</sup> and R<sup>4a</sup>, which may be the same or different, each represents

*Sub  
B<sup>1</sup>  
A<sup>t</sup>*

hydrogen or C<sub>1-3</sub>alkyl), or R<sup>5a</sup>(CH<sub>2</sub>)<sub>za</sub>X<sup>1a</sup> (wherein R<sup>5a</sup> is a 4- or 6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C<sub>1-4</sub>cynoalkyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylsulphonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>aminoalkyl, C<sub>1-4</sub>alkylamino, di(C<sub>1-4</sub>alkyl)amino, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkyl, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylaminoC<sub>1-4</sub>alkoxy, di(C<sub>1-4</sub>alkyl)aminoC<sub>1-4</sub>alkoxy and a group -(O)<sub>f</sub>(C<sub>1-4</sub>alkyl)<sub>g</sub>ringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a 4-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C<sub>1-4</sub>alkyl), za is an integer from 0 to 4 and X<sup>1a</sup> represents a direct bond, -O-, -CH<sub>2</sub>-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>6a</sup>C(O)-, -C(O)NR<sup>7a</sup>-, -SO<sub>2</sub>NR<sup>8a</sup>-, -NR<sup>9a</sup>SO<sub>2</sub>- or -NR<sup>10a</sup>- (wherein R<sup>6a</sup>, R<sup>7a</sup>, R<sup>8a</sup>, R<sup>9a</sup> and R<sup>10a</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl)); and salts thereof, and prodrugs thereof for example esters and amides, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals such as humans.

\* \* \* \* \*

Please replace the first paragraph of Example 15 at page 111, extending from line 9 to line 13, with the following amended paragraph:

*A 12*

Using a procedure analogous to that described for Example 9, 4-chloro-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline (0.13g, 0.4mmol), (prepared as described for the starting material in Example 9), was reacted with 7-hydroxy-4-methylquinoline (80mg, 0.5mol), (Chem. Berich. 1967, 100, 2077), to give **6-methoxy-4-(4-methylquinolin-7-yloxy)-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline** (155mg, 87%).

\* \* \* \* \*

Please replace the first paragraph of Example 16 at page 111, extending from line 20 to line 25, with the following amended paragraph:

A 13 Using a procedure analogous to that described for Example 9, 4-chloro-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline (0.13g, 0.4mmol), (prepared as described for the starting material in Example 9), was reacted with 2,2,4-trimethyl-1,2-dihydroquinolin-6-ol (95mg, 0.5mmol), (IZV. ACAD. NAVK. SSSR. Ser. Khim. 1981, 9, 2008), to give 6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)-4-(2,2,4-trimethyl-1,2-dihydroquinolin-6-yloxy)quinazoline (90mg, 47%).

\* \* \* \* \*

Please replace the first paragraph of Example 18 at page 112, extending from line 12 to line 16, with the following amended paragraph:

A 14 Using a procedure analogous to that described for Example 9, 4-chloro-6-methoxy-7-((1-methylpiperidin-4-yl)methoxy)quinazoline (0.13g, 0.4mmol), (prepared as described for the starting material in Example 10), was reacted with 2,4-dimethyl-7-hydroxyquinoline (87mg, 0.5mmol), (Chem. Berichte, 1903, 36, 4016), to give 4-(2,4-dimethylquinolin-7-yloxy)-6-methoxy-7-((1-methylpiperidin-4-yl)methoxy)quinazoline (61mg, 33%).

\* \* \* \* \*

Please replace the first paragraph of Example 19 at page 112, extending from line 23 to line 27, with the following amended paragraph:

A 15 Using a procedure analogous to that described for Example 9, 4-chloro-6-methoxy-7-((1-methylpiperidin-4-yl)methoxy)quinazoline (0.13g, 0.4mmol), (prepared as described for the starting material in Example 10), was reacted with 6-hydroxy-2H-4H-1,4-benzoxazin-3-one (83mg, 0.5mmol), (J. Chem. Soc. C, 1971, 2696), to give 6-methoxy-7-((1-methylpiperidin-4-yl)methoxy)-4-(3-oxo-2H-4H-1,4-benzoxazin-6-yloxy)quinazoline (158mg, 88%).

\* \* \* \* \*

Replace the first paragraph of Example 20 at page 113, extending from line 2 to line 6, with the following new paragraph:

A14 Using a procedure analogous to that described for Example 9, 4-chloro-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline (0.13g, 0.4mmol), (prepared as described for the starting material in Example 9), was reacted with 6-hydroxy-2H-4H-1,4-benzoxazin-3-one (83mg, 0.5mmol), (J. Chem. Soc. C, 1971, 2696), to give **6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)-4-(3-oxo-2H-4H-1,4-benzoxazin-6-yloxy)quinazoline** (170mg, 94%).

\* \* \* \* \*

Please replace the first paragraph of Example 71 at page 140, extending from line 12 to line 23, with the following amended paragraph:

A17 Methoxyacetaldehyde (368mg, 3.47 mmol) (freshly distilled) followed by sodium triacetoxyborohydride (552mg, 2.6mol) were added to a solution of 6-methoxy-4-(2-methylindol-5-yloxy)-7-(piperidin-4-ylmethoxy)quinazoline (726mg, 1.74mmol), (prepared as described in Example 70), in a mixture of methylene chloride (15ml) and methanol (15ml). After stirring for 1.5 hours at ambient temperature, saturated sodium hydrogen carbonate was added. The volatiles were removed under vacuum and the residue was partitioned between methylene chloride and water. The organic layer, was separated, washed with water, brine, dried ( $MgSO_4$ ) and the volatiles were removed by evaporation. The residue was purified by column chromatography eluting with methylene chloride/methanol (80/20). After removal of the solvent, the residue was triturated with ether, collected by filtration, washed with ether and dried under vacuum at 60°C to give **6-methoxy-7-(1-(2-methoxyethyl)piperidin-4-ylmethoxy)-4-(2-methylindol-5-yloxy)quinazoline** (392mg, 47%).

\* \* \* \* \*

Please replace the first paragraph of Example 90 at page 153, extending from line 4 to line 12, with the following new paragraph:

A18 A solution of 7-hydroxy-4-(2-methylindol-5-yloxy)quinazoline (423 mg, 1.45 mmol), (prepared as described for the starting material in Example 82), triphenylphosphine (685 mg, 2.61 mmol), 4-hydroxymethyl-1-*tert*-butoxycarbonylpiperidine (500 mg, 2.32 mmol), (prepared as described for the starting material in Example 10), and diisopropyl azodicarboxylate (528 mg, 2.61 mmol) in methylene chloride (18 ml) was stirred overnight at ambient temperature. The mixture was then poured onto a column of silica and eluted with ethyl acetate. After evaporation of the solvent, the residue was triturated with ether, filtered, and dried under vacuum to give **7-(1-*tert*-butoxycarbonylpiperidin-4-ylmethoxy)-4-(2-methylindol-5-yloxy)quinazoline** (478 mg, 68 %).

\* \* \* \* \*

Please replace the paragraph of Example 126 at page 168 extending from line 19 to line 24, with the following amended paragraph:

A19 A solution of 2-(piperidin-4-yl)-1-ethanol (830 mg, 6.4 mmol) in DMF (5 ml) containing tertbutyl dicarbonate anhydride (1.4 g, 6.4 mmol) was stirred at ambient temperature for 48 hours. After removal of the volatiles under vacuum, the residue was partitioned between ether and water. The organic layer was separated, washed with water, brine, dried ( $MgSO_4$ ) and evaporated to give **4-(2-hydroxyethyl)-(1-*tert*-butoxycarbonyl)piperidine** (1 g, 68 %).

\* \* \* \* \*

Please replace the first paragraph of Example 157 at page 189, extending from line 20 to line 28, with the following new paragraph: